Answers 09/24/1992

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ALZHEIMER'S DISEASE UPDATE

FDA has received inquiries about the status of therapies for Alzheimer's disease. (See talk papers T87-52, T88-27, T91-39 and T91-75.) Alzheimer's is a degenerative and fatal disease that follows a progressive course over a period of several years. It affects an estimated 4 million Americans.

The agency has approved a treatment IND for one Alzheimer's therapy -- tacrine or THA (Cognex) -- and is considering a New Drug Application for another. Health and Human Services funding for research related to Alzheimer's disease has more than doubled -- from $130.7 million in 1989 to a projected $293.5 million in 1993. In addition, officials have met with patient advocacy groups and sponsored workshops and other scientific forums to encourage further research.

The following may be used to answer questions:

Several compounds for the treatment of Alzheimer's disease are under development or testing. Among them are a group of compounds that mimic or enhance the effects of acetylcholine, affecting brain nerve pathways known to degenerate to a greater degree in Alzheimer's patients. Tacrine is one of these compounds.

In 1986 tacrine received attention as a treatment for Alzheimer's disease, based on a study reported in the New England Journal of Medicine. While the report was encouraging, the study involved only a very small

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number of patients, and much remained unknown about the drug's efficacy and safety, especially its potential for severe liver toxicity.

In July 1991, FDA's independent advisory committee met to consider an application from the Warner-Lambert Co. for approval of tacrine for patients with Alzheimer's disease. The committee recommended that the drug not be approved at that time on the basis of available data but that further studies be conducted and expanded access afforded through a Treatment IND.

In December 1991, FDA approved the Treatment IND on the basis that the drug at low doses appeared to produce a small improvement in mental function in some patients and that there was some reason to believe larger doses, which were under study, might be more effective. The Treatment IND is subject to monitoring and recordkeeping and requires that further controlled studies also be conducted.

The Treatment IND may enroll up to 15,000 patients who receive the drug at increasingly higher doses, up to a maximum of 120 mg. per day. Approximately 2,800 patients are currently enrolled. Since data on the efficacy of the drug at doses of 40 and 80 mg. were not convincing, the accompanying controlled trial will include doses of up to 160 mg., in an attempt to determine if they would be helpful in treating some or all patients. Results of the controlled trial are expected to be available within the next year.

One other New Drug Application for an Alzheimer's drug -- velnacrine (Mentane), developed and tested by Hoechst-Roussel Co., of Somerville, N.J. -- has been submitted to FDA.

The agency is keenly aware of certain patients' desires to import and use unapproved drugs for treating Alzheimer's and has therefore allowed such "personal use" importations of tacrine on a case-by-case basis. These

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have been allowed on a one-time basis with assurances by the patient and physician that the patient will be closely monitored to detect potential serious side effects. However, the agency discourages the importation of tacrine from unapproved sources, preferring instead that patients be encouraged to enroll in the treatment IND.

FDA Commissioner David A. Kessler, M.D., met with representatives of Alzheimer's patient advocate organizations on Sept. 9, 1992. Dr. Kessler reiterated his commitment to providing expanded access to tacrine, as long as patients are monitored appropriately and programs are conducted so that data can be collected to evaluate the drug's safety and effectiveness.

FDA is looking forward to increased contact with these and other Alzheimer's groups. Based on its experience with AIDS and cancer patient advocacy groups, the agency believes that more communication will lead to increased mutual understanding and progress in dealing with this life-threatening disease.